

Notice of Allowability

Application No.

10/613,754

Examiner

Andrew D. Kosar

Applicant(s)

OLSSON ET AL.

Art Unit

1654

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 7/28/05.
2. ☒ The allowed claim(s) is/are 49-78.
3. ☒ The drawings filed on 02 July 2003 are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☐ All b) ☐ Some* c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
 6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☐ including changes required by the Notice of Draftperson's Patent Drawing Review (PTO-948) attached
 - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
 - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|---|---|
| 1. <input type="checkbox"/> Notice of References Cited (PTO-892) | 5. <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 2. <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 6. <input checked="" type="checkbox"/> Interview Summary (PTO-413),
Paper No./Mail Date _____. |
| 3. <input type="checkbox"/> Information Disclosure Statements (PTO-1449 or PTO/SB/08),
Paper No./Mail Date _____ | 7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment |
| 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit
of Biological Material | 8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance |
| | 9. <input type="checkbox"/> Other _____. |

EXAMINER'S AMENDMENT/REASONS FOR ALLOWANCE

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with David J. Aston on August 4, 2005.

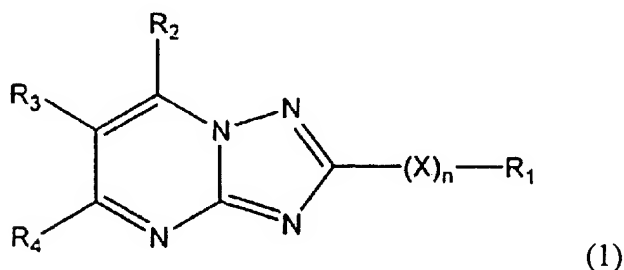
The application has been amended as follows:

Cancel claims 1-48. Add new claims 49-78 as follows:

49. (NEW) A pharmaceutical composition comprising in an effective amount for modulating EPO-R activity:

a non-peptide organic molecule of from 12 to 36 atoms other than hydrogen, from 9 to 20 carbon atoms, from 4 to 12 of the heteroatoms chalcogen, nitrogen, halogen, and metal ion of Groups I or II of the periodic chart,

wherein said non-peptide organic molecule is of the formula (1):



wherein:

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X is of from 1 to 3 atoms other than hydrogen, and is amino, alkyl substituted amino, oxygen, or sulfur bonded to 0 to 2 oxygen atoms;

n is 0 or 1;

R₁ is substituted phenyl having from 0 to 3 substituents that are CH₃, Cl, NO₂, or CF₃, and R₁ is optionally bonded directly to an annular carbon atom or through a linking group of from 1 to 3 carbon and nitrogen atoms or N-hydroxyamidinyl;

R₂ is CH₃, NH₂, OH, or aroylamido of from 7 to 8 carbon atoms having optional substituents that are CH₃, Cl, NO₂, or CF₃;

R₃ is H, carboxy, or unsubstituted or halo substituted cycloalkylalkyl of from 4 to 8 carbon atoms, having from 3 to 4 annular atoms;

R₄ is H, unsubstituted or halo substituted lower alkyl of from 1 to 3 carbon atoms, or alkoxymethyl of from 2 to 4 carbon atoms;

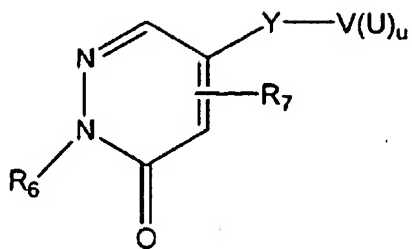
with the proviso that R₃ and R₄ may be taken together to define 1,2-dimethylene-alpha-halo, or alpha-CH₃-halobenzene, where halo is F or Cl; and
a pharmaceutically acceptable vehicle.

50. (NEW) A pharmaceutical composition comprising in an effective amount for modulating EPO-R activity:

a non-peptide organic molecule of from 12 to 36 atoms other than hydrogen, from 9 to 20 carbon atoms, from 4 to 12 of the heteroatoms chalcogen, nitrogen, halogen, and metal ion of Groups I or II of the periodic chart,

wherein said non-peptide organic molecule is of the formula (3):

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(3)

wherein:

Y is amino, CH₂, O, or S(O)_m, where m is 0, 1 or 2;

R₆ is H or alkyl of from 1 to 3 carbon atoms;

R₇ is H, or a group of from 0 to 3 atoms other than hydrogen, and is oxy, thio, amino, nitro, cyano or alkyl;

V is a phenyl group;

U is a group of from 0 to 3 atoms other than hydrogen, and is oxy, thio, amino, nitro, cyano, halo or alkyl;

u is 0 to 3; and

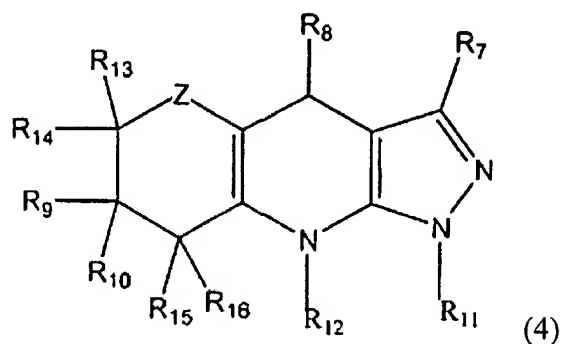
a pharmaceutically acceptable vehicle.

51. (NEW) A pharmaceutical composition comprising in an effective amount for modulating EPO-R activity:

a non-peptide diazohydroquinoline organic molecule of from 12 to 36 atoms other than hydrogen, from 9 to 20 carbon atoms, from 4 to 12 of the heteroatoms chalcogen, nitrogen, halogen, and metal ion of Groups I or II of the periodic chart,

wherein said non-peptide diazohydroquinoline organic molecule is of the formula (4):

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wherein:

Z is CH₂, C=O, C=S, C=NH, or CH-alkyl, wherein alkyl is of from 1 to 3 carbon atoms;

R₇ is H or an organic group of from 1 to 12 carbon atoms and 0 to 4 heteroatoms;

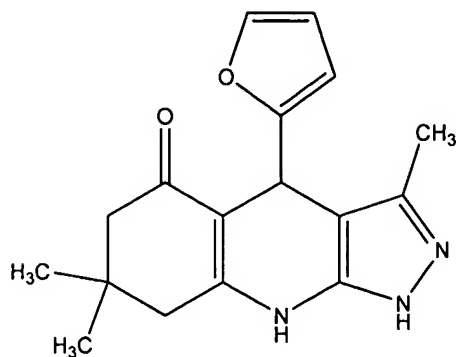
R₈ is H, an aliphatic group of from 1 to 6 carbon atoms, or a heterocycle of from 5 to 6 annular members and from 1 to 2 heteroannular members that are O, N, or S;

R₉, R₁₀, R₁₃, R₁₄, R₁₅ and R₁₆ are the same or different and are H, an organic radical of from 1 to 12 carbon atoms or a heterosubstituent of from 1 to 3 heteroatoms;

R₁₁ and R₁₂ are the same or different and are H or an organic group of from 1 to 12 carbon atoms; and

a pharmaceutically acceptable vehicle.

52. (NEW) The pharmaceutical composition according to claim 51, wherein said diazoloquinoline is of the formula:

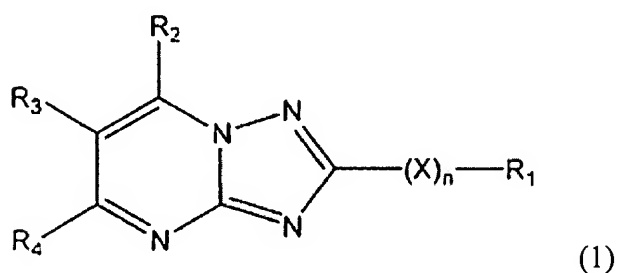


53. (NEW) An EPO receptor complex having a polypeptide comprising:

the modulating domain sequence of erythropoietin receptor; and

a non-peptide organic molecule of from 12 to 36 atoms other than hydrogen, from 9 to 20 carbon atoms, from 4 to 12 of the heteroatoms chalcogen, nitrogen, halogen, and metal ion of Groups I or II of the periodic chart,

wherein said non-peptide organic molecule is of the formula (1):



wherein:

X is of from 1 to 3 atoms other than hydrogen, and is amino, alkyl substituted amino, oxygen, or sulfur bonded to 0 to 2 oxygen atoms;

n is 0 or 1;

R₁ is alkyl of from 1 to 3 carbon atoms, or an organic group having a six annular membered aromatic group having from 0 to 3 substituents, where the substituents are halo, lower alkyl of from 1 to 3 carbon atoms, NO₂, or

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trihalomethyl, and R_1 is bonded directly to X or bonded through a linking group of from 1 to 4 carbon, nitrogen, or chalcogen atoms in a chain, there being from 0 to 2 heteroatoms in the chain, where the heteroatoms are bonded solely to carbon and hydrogen, or alpha-acetamidinyl having from 0 to 1 N-OH;

R_2 is H, alkylamino of from 0 to 3 carbon atoms, alkoxy of from 0 to 3 carbon atoms, or a heterofunctionality having nitrogen or chalcogen bonded to annular carbon which is substituted with an organic group of from 1 to 10 carbon atoms and from 0 to 3 heteroatoms;

R_3 is H or an organic group of from 1 to 10 carbon atoms and from 0 to 4 chalcogen, halo or nitrogen heteroatoms;

R_4 is H, or optionally substituted alkyl of from 1 to 6 carbon atoms, where the substituents are oxy, amino or halo;

with the proviso that R_3 and R_4 may be taken together to form a ring with the annular atoms to which they are attached of from 4 to 10 annular atoms and forming from 1 to 2 rings, where the annular atoms are unsubstituted or substituted with halo, alkyl of from 1 to 3 carbon atoms, alkoxy of from 0 to 3 carbon atoms, thioalkyl of from 0 to 3 carbon atoms, or alkyl amino of from 0 to 4 carbon atoms.

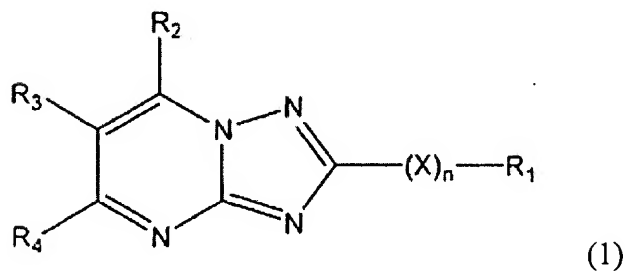
54. (NEW) The complex according to claim 53, wherein R_3 is H or an organic group of from 1 to 8 carbon atoms and 0 to 4 chalcogen, halo, or nitrogen heteroatoms.

55. (NEW) The complex according to claim 54, wherein R_3 is cyclopropylmethylamino.

56. (NEW) The complex according to claim 54, wherein R_3 is H.

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57. (NEW) The complex according to claim 54, wherein R_1 is a six annular membered aromatic group having 0 to 3 substituents, where the substituents are halo, lower alkyl of from 1 to 3 carbon atoms, nitro or trihalomethyl, and is either directly bonded to X or bonded through a linking group of from 1 to 4 carbon, nitrogen, or chalcogen atoms in a chain.
58. (NEW) The complex according to claim 54, wherein R_4 is methyl.
59. (NEW) The complex according to claim 54, wherein R_4 is H.
60. (NEW) An EPO receptor complex having a polypeptide comprising:
the modulating domain sequence of erythropoietin receptor; and
a non-peptide organic molecule of from 12 to 36 atoms other than hydrogen, from 9 to 20 carbon atoms, from 4 to 12 of the heteroatoms chalcogen, nitrogen, halogen, and metal ion of Groups I or II of the periodic chart,
wherein said non-peptide organic molecule is of the formula (1):



wherein:

- X is from 1 to 7 atoms other than hydrogen, and is amino, alkyl substituted amino, oxygen, or sulfur bond bonded to 0 to 2 oxygen atoms;
- n is 0 or 1;
- R_1 is alkyl of from 1 to 3 carbon atoms, or substituted phenyl having from 0 to 3 substituents that are CH_3 , Cl, NO_2 , or CF_3 , and R_1 is bonded directly to an

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annular carbon atom or through a linking group of from 1 to 3 carbon and nitrogen atoms or N-hydroxyamidinyl;

R_2 is CH_3 , NH_2 , OH , or aroylamido of from 7 to 8 carbon atoms having substituents that are CH_3 , Cl , NO_2 , or CF_3 ;

R_3 is H, carboxy, or unsubstituted or halo substituted cycloalkylalkyl of from 4 to 8 carbon atoms, having from 3 to 4 annular atoms;

R_4 is H, unsubstituted or halo substituted lower alkyl of from 1 to 3 carbon atoms, or alkoxymethyl of from 2 to 4 carbon atoms;

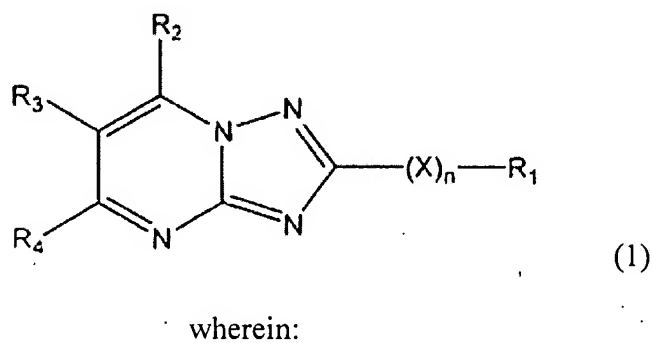
With the proviso that R_3 and R_4 may be taken together to define 1,2-dimethylene- α -halo, or α - CH_3 -halobenzene, where halo is F or Cl.

61. (NEW) An EPO receptor complex having a polypeptide comprising:

the modulating domain sequence of erythropoietin receptor; and

a non-peptide organic molecule of from 12 to 36 atoms other than hydrogen, from 9 to 20 carbon atoms, from 4 to 12 of the heteroatoms chalcogen, nitrogen, halogen, and metal ion of Groups I or II of the periodic chart,

wherein said non-peptide organic molecule is of the formula:



X is from 1 to 7 atoms other than hydrogen, and is amino, alkyl substituted amino, oxygen, or sulfur bond bonded to 0 to 2 oxygen atoms;

n is 0 or 1;

R₁ is organic group of from 1 to 12 carbon atoms and from 0 to 6 heteroatoms, which are chalcogen, nitrogen, or halogen, said organic group further comprising an aliphatic group of from 1 to 6 carbon atoms having from 0 to 2 sites of unsaturation, non-oxo-carbonyl and the nitrogen and sulfur derivatives thereof, alicyclic group having from 0 to 2 sites of unsaturation, aryl group, heterocyclic group and combinations thereof, where the cyclic structures may have from 1 to 2 rings;

R₂ is H, a heterofunctionality having nitrogen and/or chalcogen bonded to annular carbon to which is substituted with an organic group of from 1 to 10 carbon atoms, aryl, alkaryl, aralkyl, and aralkenyl of from 5 to 10 carbon atoms, aroyl of from 6 to 10 carbon atoms, or an organic group bonded through a carbon atom of from 1 to 12 carbon atoms having from 1 to 4 heteroatoms, which are chalcogen, nitrogen, or halogen;

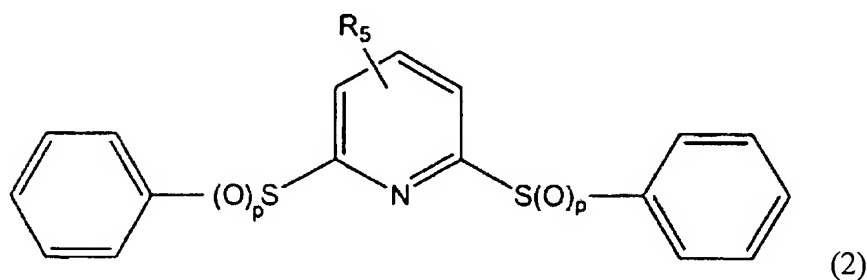
R₃ is H or an organic group of from 1 to 10 carbon atoms and from 0 to 4 chalcogen and nitrogen heteroatoms;

R₄ is H, alkyl, or substituted alkyl of from 1 to 6 carbon atoms, where the substituents are oxy, amino or halo;

With the proviso that R₃ and R₄ may be taken together to form a ring with the annular atoms to which they are attached of from 4 to 10 annular atoms and

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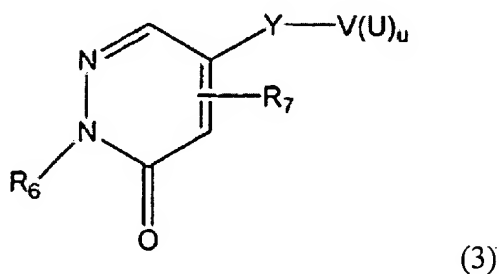
forming from 1 to 2 rings, where the annular atoms are unsubstituted or substituted with halo, alkyl of from 1 to 3 carbon atoms, alkoxy of from 0 to 3 carbon atoms, thioalkyl of from 0 to 3 carbon atoms and alkylamino of from 0 to 4 carbon atoms;



wherein:

p is 0, 1, or 2;

R_5 has from 1 to 3 atoms other than hydrogen, and is oxy, thio, amino, nitro, cyano, or alkyl;



wherein:

Y is amino, CH_2 , O, or S(O)_m , wherein m is 0, 1, or 2;

V is an aryl group having 6 annular members comprising 0 to 2 nitrogen atoms, the remainder being carbon atoms;

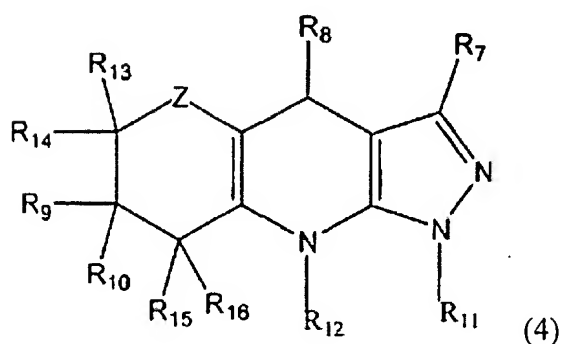
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U is a substituent of from 0 to 5 atoms other than H, and is oxy, thio, amino, nitro, cyano, halo, or alkyl;

u is 0 to 3;

R₆ is H or alkyl of from 1 to 3 carbon atoms;

R₇ is H or a group having 0 to 3 atoms other than H, and is oxy, thio, amino, nitro, cyano, or alkyl; or



wherein:

Z is CH₂, C=O, C=S, C=NH, or CH-alkyl, wherein alkyl is of from 1 to 3 carbon atoms;

R₇ is H or an organic group of from 1 to 12 carbon atoms and 0 to 4 heteroatoms;

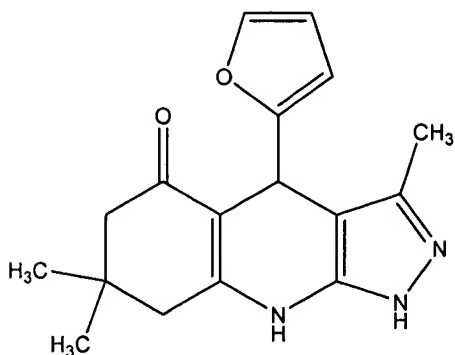
R₈ is H, an aliphatic group of from 1 to 6 carbon atoms, or a heterocycle of from 5 to 6 annular members and from 1 to 2 heteroannular members that are O, N, or S;

R₉, R₁₀, R₁₃, R₁₄, R₁₅ and R₁₆ are the same or different and are H, an organic radical of from 1 to 12 carbon atoms or a heterosubstituent of from 1 to 3 heteroatoms;

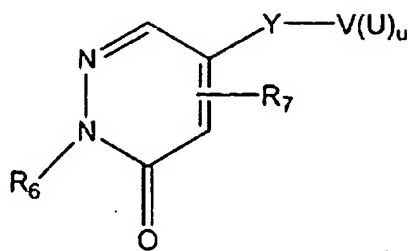
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R_{11} and R_{12} are the same or different and are H or an organic group of from 1 to 12 carbon atoms.

62. (NEW) A complex according to claim 61, wherein said polypeptide and said non-peptide organic molecule are complexed at the modulating domain of EPO-R.
63. (NEW) A complex according to claim 62, wherein said polypeptide is EPO-R bound to a cellular membrane.
64. (NEW) A complex according to claim 61, wherein the non-peptide organic molecule is a diazoloheptahydroquinoline of formula (4).
65. (NEW) A complex according to claim 64, wherein the diazoloheptahydroquinoline is of the formula:



66. (NEW) An EPO receptor complex having a polypeptide comprising:
the modulating domain sequence of erythropoietin receptor; and
a non-peptide organic molecule of from 12 to 36 atoms other than hydrogen, from 9 to 20 carbon atoms, from 4 to 12 of the heteroatoms chalcogen, nitrogen, halogen, and metal ion of Groups I or II of the periodic chart,
wherein said non-peptide organic molecule is of the formula:



(3)

wherein:

Y is amino, CH₂, O, or S(O)_m, where m is 0, 1 or 2;

R₆ is H or alkyl of from 1 to 3 carbon atoms;

R₇ is H, or a group of from 0 to 3 atoms other than hydrogen, and is oxy, thio, amino, nitro, cyano or alkyl;

V is a phenyl group;

U is a group of from 0 to 3 atoms other than hydrogen, and is oxy, thio, amino, nitro, cyano, halo or alkyl; and

u is 0 to 3.

67. (NEW) The complex according to claim 66, wherein Y is SO₂, R₇ is Cl, and u is 0.

68. (NEW) A method for determining the binding affinity of a test compound to the modulating domain of EPO-R, said method comprising:

adding said test compound to a complex according to claim 61; and

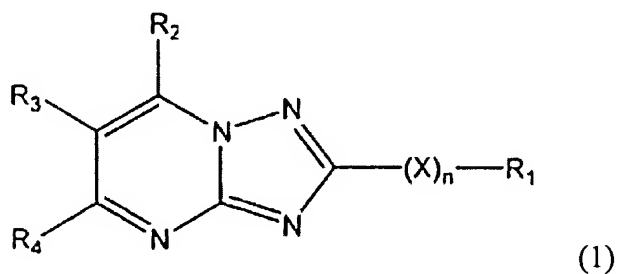
determining the amount of complex of said complex in the presence of said test compound as compared to the absence of said test compound.

69. (NEW) A method of inducing a physiological response of EPO-R in a host, the method comprising:

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administering to said host a physiologically effective amount of a non-peptide organic molecule of from 12 to 36 atoms other than hydrogen, from 9 to 20 carbon atoms, from 4 to 12 of the heteroatoms chalcogen, nitrogen, halogen, and metal ion of Groups I or II of the periodic chart,

wherein said non-peptide organic molecule is of the formula:



wherein:

X is of from 1 to 3 atoms other than hydrogen, and is amino, alkyl substituted amino, oxygen, or sulfur bonded to 0 to 2 oxygen atoms;

n is 0 or 1;

R₁ is alkyl of from 1 to 3 carbon atoms, substituted phenyl having from 0 to 3 substituents that are CH₃, Cl, NO₂, or CF₃, and R₁ is bonded directly to an annular carbon atom or through a linking group of from 1 to 3 carbon and nitrogen atoms in a chain, or N-hydroxamindinyl;

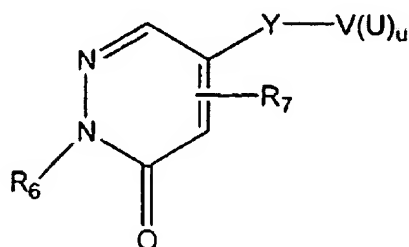
R₂ is CH₃, NH₂, OH, or aroylamido of from 7 to 8 carbon atoms having from 0 to 2 substituents that are CH₃, Cl, NO₂, or CF₃;

R₃ is H, carboxy, or cycloalkylalkyl of from 4 to 8 carbon atoms, having from 3 to 4 annular atoms;

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R_4 is H, unsubstituted or halo substituted lower alkyl of from 1 to 3 carbon atoms, or alkoxymethyl of from 2 to 4 carbon atoms;

with the proviso that R_3 and R_4 may be taken together to define 1,2-dimethylene- α -halo, or α -CH₃-halobenzene, where halo is F or Cl; or



(3)

wherein:

Y is amino, CH₂, O, or S(O)_m, where m is 0, 1 or 2;

R_6 is H or alkyl of from 1 to 3 carbon atoms;

R_7 is H, or a group of from 0 to 3 atoms other than hydrogen, and is oxy, thio, amino, nitro, cyano or alkyl;

V is a phenyl group;

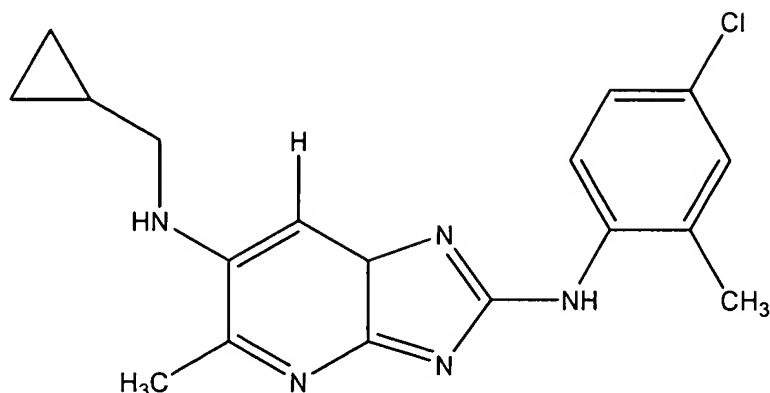
U is a group of from 0 to 3 atoms other than hydrogen, and is oxy, thio, amino, nitro, cyano, halo or alkyl; and

u is 0 to 3.

70. (NEW) A method according to claim 69, wherein the non-peptide organic molecule is of formula (1).

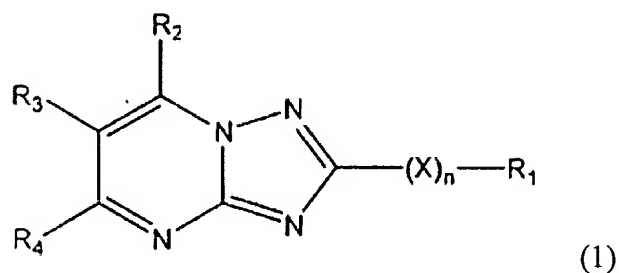
71. (NEW) A method according to claim 70, wherein the non-peptide organic molecule is of the formula:

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72. (NEW) A method of modulating the response to a stimulus of hematopoietic or neuronal cells influenced by the binding of EPO to EPO-R, the method comprising:
 contacting said cells with an effective amount to modulate said response of a non-peptide organic molecule of from 12 to 36 atoms other than hydrogen, from 9 to 20 carbon atoms, from 4 to 12 of the heteroatoms chalcogen, nitrogen, halogen, and metal ion of Groups I or II of the periodic chart,

wherein said non-peptide organic molecule is of the formula:



wherein:

X is of from 1 to 3 atoms other than hydrogen, and is amino, alkyl

substituted amino, oxygen, or sulfur bonded to 0 to 2 oxygen atoms;

n is 0 or 1;

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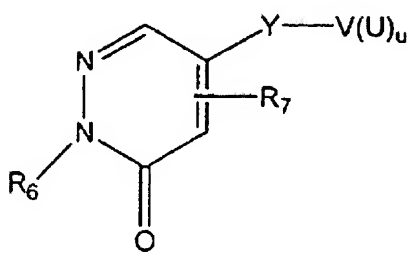
R_1 is alkyl of from 1 to 3 carbon atoms, substituted phenyl having from 0 to 3 substituents that are CH_3 , Cl , NO_2 , or CF_3 , and R_1 is bonded directly to an annular carbon atom or through a linking group of from 1 to 3 carbon and nitrogen atoms in a chain, or N-hydroxamidinyl;

R_2 is CH_3 , NH_2 , OH , or aroylamido of from 7 to 8 carbon atoms having from 0 to 2 substituents that are CH_3 , Cl , NO_2 , or CF_3 ;

R_3 is H, carboxy, or cycloalkylalkyl of from 4 to 8 carbon atoms, having from 3 to 4 annular atoms;

R_4 is H, unsubstituted or halo substituted lower alkyl of from 1 to 3 carbon atoms, or alkoxymethyl of from 2 to 4 carbon atoms;

with the proviso that R_3 and R_4 may be taken together to define 1,2-dimethylene- α -halo, or α - CH_3 -halobenzene, where halo is F or Cl; or



(3)

wherein:

Y is amino, CH_2 , O , or $\text{S}(\text{O})_m$, where m is 0, 1 or 2;

R_6 is H or alkyl of from 1 to 3 carbon atoms;

R_7 is H, or a group of from 0 to 3 atoms other than hydrogen, and is oxy, thio, amino, nitro, cyano or alkyl;

V is a phenyl group;

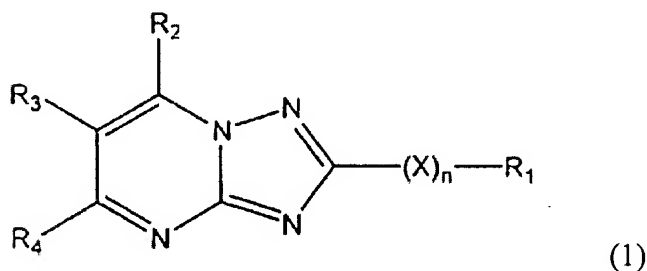
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U is a group of from 0 to 3 atoms other than hydrogen, and is oxy, thio, amino, nitro, cyano, halo or alkyl; and

u is 0 to 3.

73. (NEW) A method for modulating the activity of EPO-R, present in a cell membrane component, comprising:
forming an EPO-R: non-peptide organic molecule complex in said cell membrane by contacting said EPO-R with an effective amount of a non-peptide organic molecule of from 12 to 36 atoms other than hydrogen, from 9 to 20 carbon atoms, from 4 to 12 of the heteroatoms chalcogen, nitrogen, halogen, and metal ion of Groups I or II of the periodic chart,

wherein said non-peptide organic molecule is of the formula:



wherein:

X is from 1 to 7 atoms other than hydrogen, and is amino, alkyl substituted amino, oxygen, or sulfur bond bonded to 0 to 2 oxygen atoms;

n is 0 or 1;

R₁ is H or an organic group of from 1 to 12 carbon atoms and from 0 to 6 heteroatoms, which are chalcogen, nitrogen, or halogen, said organic group further comprising an aliphatic group of from 1 to 6 carbon atoms having from 0

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to 2 sites of unsaturation, non-oxo-carbonyl and the nitrogen and sulfur derivatives thereof, alicyclic group having from 0 to 2 sites of unsaturation, aryl group, heterocyclic group and combinations thereof, where the cyclic structures may have from 1 to 2 rings;

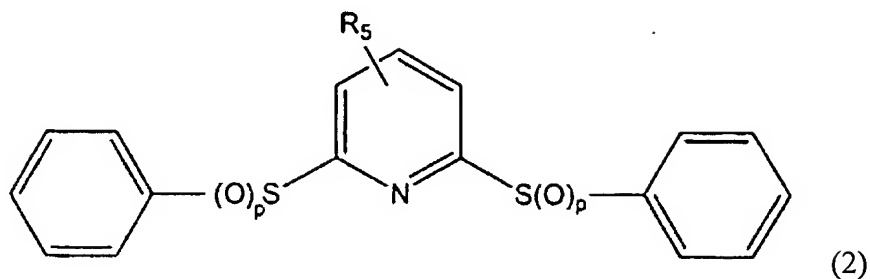
R_2 is H, a heterofunctionality having nitrogen and/or chalcogen bonded to annular carbon to which is substituted with an organic group of from 1 to 10 carbon atoms, aryl, alkaryl, aralkyl, and aralkenyl of from 5 to 10 carbon atoms, aroyl of from 6 to 10 carbon atoms, or an organic group bonded through a carbon atom of from 1 to 12 carbon atoms having from 1 to 4 heteroatoms, which are chalcogen, nitrogen, or halogen;

R_3 is H or an organic group of from 1 to 10 carbon atoms and from 0 to 4 chalcogen and nitrogen heteroatoms;

R_4 is H, alkyl, or substituted alkyl of from 1 to 6 carbon atoms, where the substituents are oxy, amino or halo;

With the proviso that R_3 and R_4 may be taken together to form a ring with the annular atoms to which they are attached of from 4 to 10 annular atoms and forming from 1 to 2 rings, where the annular atoms are unsubstituted or substituted with halo, alkyl of from 1 to 3 carbon atoms, alkoxy of from 0 to 3 carbon atoms, thioalkyl of from 0 to 3 carbon atoms or alkylamino of from 0 to 4 carbon atoms;

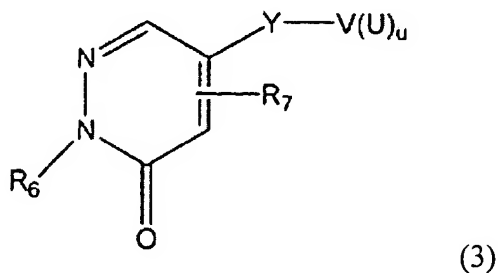
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wherein:

 p is 0, 1, or 2;

R_5 has from 1 to 3 atoms other than hydrogen, and is oxy, thio, amino, nitro, cyano, or alkyl;



wherein:

 Y is amino, CH_2 , O, or $S(O)_m$, wherein m is 0, 1, or 2;

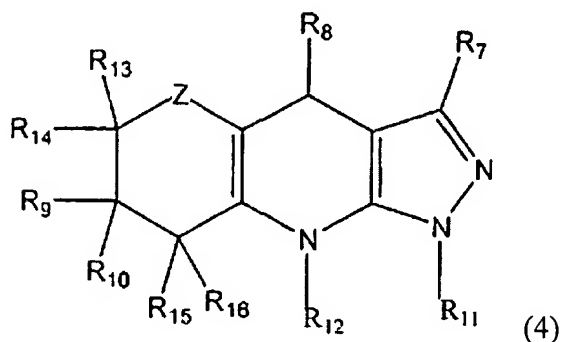
V is an aryl group having 6 annular members comprising 0 to 2 nitrogen atoms, the remainder being carbon atoms;

U is a substituent of from 0 to 5 atoms other than H, and is oxy, thio, amino, nitro, cyano, halo, or alkyl;

 u is 0 to 3; R_6 is H or alkyl of from 1 to 3 carbon atoms;

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R_7 is H or a group having 0 to 3 atoms other than H, and is oxy, thio, amino, nitro, cyano, or alkyl; or



wherein:

Z is CH_2 , $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{C}=\text{NH}$, or C-alkyl, wherein alkyl is of from 1 to 3 carbon atoms;

R_7 is H or an organic group of from 1 to 12 carbon atoms and 0 to 4 heteroatoms;

R_8 is H, an aliphatic group of from 1 to 6 carbon atoms, or a heterocycle of from 5 to 6 annular members and from 1 to 2 heteroannular members that are O, N, or S;

R_9 , R_{10} , R_{13} , R_{14} , R_{15} and R_{16} are the same or different and are H, an organic radical of from 1 to 12 carbon atoms or a heterosubstituent of from 1 to 3 heteroatoms;

R_{11} and R_{12} are the same or different and are H or an organic group of from 1 to 12 carbon atoms.

74. (NEW) The method of claim 73, wherein the non-peptide organic molecule is of formula (1).

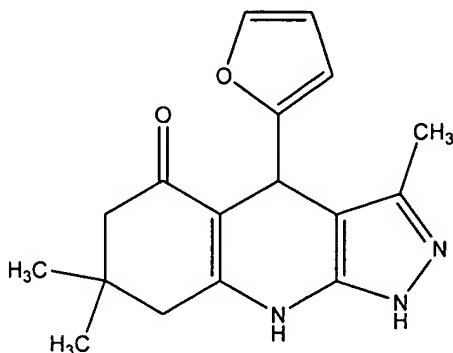
75. (NEW) The method of claim 73, wherein the non-peptide organic molecule is of formula (2).

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76. (NEW) The method of claim 73, wherein the non-peptide organic molecule is of formula (3).

77. (NEW) The method of claim 73, wherein the non-peptide organic molecule is a diazohexahydroquinoline of formula (4).

78. (NEW) The method of claim 77, wherein said diazohexahydroquinoline is of the formula:



Reasons for Allowance

The following is an examiner's statement of reasons for allowance: The prior art of record does not teach or suggest, alone or in combination, the instantly claimed pharmaceuticals or their methods of use.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew D. Kosar whose telephone number is (571)272-0913. The examiner can normally be reached on Monday - Friday 8am-430pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571)272-0974. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Andrew D. Kosar, Ph.D.
Art Unit 1654



CHRISTOPHER R. TATE
PRIMARY EXAMINER